

REMARKS

Claims 1-18 were pending in this application.

The Examiner made the following objections and rejections in the non-final Office Action mailed July 12, 2006:

- 1) The Examiner alleges the instant C.I.P. application is not entitled to its earliest priority date.
- 2) The Examiner objects to the Applicants' formatting of a trademark in the specification.
- 3) The Examiner objects to claims 4, 12, 14 and 15 as reciting: i) non-elected subject matter, and ii) an undefined acronym.
- 4) The Examiner rejects claims 1, 2, 4 and 6 in view of statutory type double patenting.
- 5) The Examiner rejects claims 10-18 under 35 U.S.C. §112 (second paragraph) as being indefinite for failing to particularly point out and distinctly claim the subject matter which the Applicants regard as the invention.
- 6) The Examiner rejects claims 1, 2, 4, 6 and 10-18 under 35 U.S.C. §112 (first paragraph) as failing to comply with the written description requirement.
- 7) The Examiner rejects claims 1, 2, 4, 6, 10, 11, 13 and 16 as anticipated (separately) by U.S. Patent 6,232,071 to Hicke *et al.*, WO 99/30561 to Warren, and U.S. publication 2003/0049203 to Elmaleh *et al.*.
- 8) The Examiner rejects claims 1, 2, 4, 6 and 10-18 under 35 U.S.C. §103(a) over WO 99/30561 to Warren in view of Holmes (Expert Opinion on Investigational Drugs, 2001), Apelgren *et al.* (Cancer Research, 1990) and U.S. Patent 5,997,861 to Virtanen *et al.*.

The Applicants believe the present amendments, and the following remarks, traverse the Examiner's rejections. These remarks are presented in the same order as they appear above.

1. The Applicants Priority Claim Is Correct

The Examiner alleges that the prior filed application, U.S. Application Serial No.: 10/600,007 (now abandoned), does not provide support for aptamer-drug conjugates having the formula shown in claim 10, nor does it provide support for aptamer-drug conjugates comprising DAVCH, Boc-protected amines, dendrimers or comb polymers. The Applicants disagree. Moreover, the Applicants note the instant application claims priority to U.S. application Serial No.: 60/390,042, filed on June 18, 2002. In this respect, the Applicants assert the claimed embodiments of the present invention should enjoy this June 18, 2002 priority date. The Examiner is reminded that matter disclosed in the parent application is entitled to the benefit of the filing date of the parent application. See, Waldemar Link, GmbH & Co. v. Osteonics Corp., 31 USPQ 2d 1855, 1857 (Fed. Cir. 1994). The Applicants provided, in U.S. application Serial No.: 60/390,042 filed on June 18, 2002, a comprehensive teaching regarding aptamer-drug conjugates. In view of these teachings, in the aforementioned provisional application, the Applicants respectfully submit that all pending claims are entitled to this June 18, 2002 priority date.

2. Applicants Use “SELEX” As An Acronym And Not As A Trademark

The Applicants refer to SELEX, in the instant application, as an acronym for: “Systematic Evolution of Ligands by Exponential Enrichment.” That is to say, they are not referring to SELEX as a trademark. Therefore, at this stage of the prosecution, the Applicants decline to re-format SELEX as a trademark (i.e. SELEX). However upon allowance of any claims the Applicants are willing, in order to expedite the issue of a patent, to file a substitute specification compliant with MPEP 608.01(v).

3. The Claims Recite No Non-Elected Subject Matter

The Examiner objected to claims 4, 12, 14 and 15 as reciting non-elected subject matter. The Applicants have amended the claims consistent with their election made in the Office Action response filed on April 24, 2006. The Applicants respectfully submit, therefore, the Examiner’s objection is moot.

4. The Rejection In View Of Statutory-Type Double Patenting Is Moot

The Examiner provisionally rejects, under 35 U.S.C. §101, claims 1, 2, 4 and 6 of the instant application as claiming the same invention recited in claims 1, 2, 4 and 6 of U.S. patent application Serial No. 10/600,007. The Applicants note U.S. patent application Serial No. 10/600,007 is, now, abandoned. See, Notice of Abandonment mailed November 14, 2006. Given U.S. patent application Serial No. 10/600,007 is abandoned, the Applicants respectfully submit the pending statutory-type double patenting rejection is moot.

5. The Rejections Raised Under 35 U.S.C. §112, Second Paragraph, Are Moot

In order to further business interests and without acquiescing to any of the arguments raised by the Examiner, the Applicants have (while expressly reserving the right to prosecute the claims as originally filed, or claims similar thereto, in a subsequently filed application) amended claim 10. Now, in the formula: “(aptamer)n -- linker -- (drug)m,” m is defined in a range between 1 - 20. The Applicants submit the pending rejection raised in view of 35 U.S.C. §112 (Second Paragraph) is now moot and, therefore, should be withdrawn.

6. The Claims Satisfy 35 U.S.C. §112, First Paragraph

Claims 1, 2, 4, 6 and 10-18 are rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Examiner states that these claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. More specifically, the Examiner alleges the lack of specific sequence(s) for an anti-PSMA aptamer amounts to a lack of written description for the claimed embodiments of the present invention. Office Action mailed 07/12/2006, p. 7. The Examiner is reminded that *ipsis verbis* disclosure is not necessary to satisfy the written description requirement

of section 112. Instead, the disclosure need only reasonably convey to persons skilled in the art that the inventors had possession of the subject matter in question. See, *In re Edwards*, 568 F.2d 1349, 1351-52, 196 USPQ 465, 467 (CCPA 1978) and *Fujikawa v. Wattanasin*, 39 USPQ 2D 1895, 1904 (Fed. Cir. 1996).

In this respect, the Applicants have provided an exhaustive disclosure with regard to aptamer selection. In one example, the Applicants provide a detailed description of the SELEX process between paragraphs [0091] and [00169] in the application as filed. This SELEX process describes the protocols required to generate aptamers against a variety of targets including PSMA. Therefore, the Applicants submit the pending rejection raised in view of 35 U.S.C. §112 (first paragraph) should be withdrawn.

7. The Claims are Not Anticipated

The Examiner has rejected claims 1, 2, 4, 6, 10, 11, 13 and 16 under 35 U.S.C. §102(b) as anticipated, separately, by U.S. Patent 6,232,071 to Hicke *et al.* and Warren, WO 99/30561. In addition claim 1 is also rejected, under 35 U.S.C. §102(e), as anticipated by US 2003/0049203 to Elmaleh *et al.* The Applicants respectfully disagree.

The MPEP states that "to anticipate a claim, the reference must teach *every* element of the claim." MPEP § 2131 (emphasis added). In order to further business interests and without acquiescing to any of the arguments raised by the Examiner, the Applicants have (while expressly reserving the right to prosecute the claims as originally filed, or claims similar thereto, in a subsequently filed applications) amended the two pending independent claims (i.e. claims 1 and 10). Specifically, the Applicants have defined the aptamer-toxin / aptamer-drug conjugates as comprising an aptamer specific for PSMA (Prostate Specific Membrane Antigen). All of the 102 art cited by the Examiner is silent on an aptamer-toxin or aptamer-drug conjugate comprising an aptamer directed against PMSA. The Examiner tacitly admits the same by failing to hold claim 12 as anticipated by the art cited. Given that Hicke *et al.*, Warren, and Elmaleh *et al.* are all silent on this element, included in all the pending claims, these references cannot anticipate the claimed embodiments of the present invention. See, *Atlas Powder Co. v.*

E.I. du Pont De Nemours & Co., 224 U.S.P.Q. 409, 411 (Fed. Cir. 1984). The Applicants, therefore, respectfully request the pending rejections, raised under 35 U.S.C. §102(b) and (e), be withdrawn.

8. The Claims Are Not Obvious

A. The Examiner Fails to Make a *Prima Facie* Case of Obviousness

The Examiner is reminded that a *prima facie* case of obviousness requires citation to a combination of references which (a) disclose the elements of the claimed invention, (b) suggests or motivates one of skill in the art to combine the elements to yield the claimed combination, and (c) provides a reasonable expectation of success should the claimed combination be carried out. Failure to establish any one of these three requirements precludes a finding of a *prima facie* case of obviousness, and, without more, entitles Applicants to allowance of the claims in issue. See, e.g., *Northern Telecom Inc. v. Datapoint Corp.*, 15 U.S.P.Q.2d 1321, 1323 (Fed. Car. 1990).

The Applicants respectfully submit the Examiner has failed to establish a *prima facie* case of obviousness.

i. The Examiner Must Point to Evidence

The requirement that the Examiner make a showing of a suggestion, teaching or motivation is "an essential evidentiary component of an obviousness holding." *C.R. Bard, Inc. v. M3 Sys. Inc.*, 157 F.3d 1340, 1352 (Fed. Car. 1998). There are three sources for this evidentiary component: the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. *Pro-Mold & Tool Co. v. Great Lakes Plastics, Inc.*, 75 F.3d 1568, 1573 (Fed. Car. 1996). Nonetheless, regardless of the source of the requisite evidence, the Examiner's showing "must be clear and particular, and broad conclusory statements...standing alone, are not 'evidence'." *In re Dembiczak*, 175 F.3d 994, 1000 (Fed. Car. 1999).

Importantly, since an Examiner is not one skilled in the art (under the law), the Examiner's opinion on what one skilled in the art might believe is of no moment. *In re Rijckaert*, 9 F.3d 1531, 28 U.S.P.Q.2d 1955, 1956 (Fed. Car. 1993) ("[T]he examiner's

assumptions do not constitute the disclosure of the prior art"). Of course, if the Examiner has knowledge of relevant facts which are used to make the rejection, the Examiner is free to use those facts - but only if submitted in the form of an affidavit. In the instant prosecution the Examiner has submitted no such affidavit.

In view of the standards set out above, the Applicants submit the Examiner merely provides a synopsis of the teachings in Warren, Holmes, Apelgren and Virtanen which the Examiner then (impermissibly) attempts to cobble together, by means of opinion and conclusory statements, into the pending obviousness rejection. This does not amount to the requisite "evidence" needed to support a rejection under 35 U.S.C. §103.

For example, the Examiner asserts that:

" It would have been obvious to one of ordinary skill in the art at the time of invention to make aptamer-drug conjugates as taught by Warren using an aptamer that targets PSMA". Office Action dated 07/12/2006, p. 12.

In previous sections of this same Office Action, however, the Examiner makes the following admissions which undermine the argument set out above. First, the Examiner acknowledges the deficiencies in Warren by admitting, "Warren does not explicitly teach aptamers targeted to PSMA, the use of the vinblastine analog desacetylvinblastine-3-carboxhydrazide or the use of linkers that comprise dendrimers". Office Action dated 07/12/2006, p. 11. Then, the Examiner admits that, "[b]ecause aptamers are discovered empirically, the structures of aptamers known from the prior art to target a particular protein would not lead the skilled artisan to the structures of aptamers having the function of binding PSMA." Office Action dated 07/12/2006, p. 7. The Examiner attempts to bridge this gap by stating that, "Holmes provides a motivation to target PSMA with therapeutic agents, teaching that this protein is preferentially expressed in prostate tissue and expressed at increased levels in cancerous cells." Office Action dated 07/12/2006, p. 12. Holmes, however, is completely silent on the use of aptamers in *any* of the methodologies presented.

In sum, the Examiner admits: i) the deficiencies in Warren, ii) the empirical (i.e. non-obvious) nature of developing aptamers to a given target (i.e. PMSA) and iii) offers, nonetheless, a reference that is complexly silent on aptamers as motivation to recapitulate the aptamer-toxin conjugates as claimed in the present invention. The Applicants, therefore, submit the Examiner fails to make a *prima facie* case of obviousness and respectfully request the pending rejection under 35 U.S.C. §103 be withdrawn.

CONCLUSION

The Applicants submits the amendments and arguments set forth above traverse the Examiner's rejections and, therefore, request that these rejections be withdrawn and the pending claims be passed to allowance. Should the Examiner believe a telephone interview would aid in the prosecution of this application, the Applicants encourage the Examiner to call the undersigned collect at 617.542.6000.

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